IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:
Agrafiotis *et al.*
Appl. No. 10/058,216
Filed: January 28, 2002
For: **Method, System, and Computer Program Product for Analyzing Combinatorial Libraries**

Confirmation No. 3315
Art Unit: 1631
Examiner: Mahatan
Atty. Docket: 1503.1230001

#7
Plunkett
5/13/03

Third Supplemental Information Disclosure Statement

Director of the United States
Patent and Trademark Office
PO Box 1450
Alexandria, VA 22313-1450

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98.

Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application

does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

Applicants have checked the appropriate boxes below.

☐ 1. Statement under 37 C.F.R. 1.704(d). Each item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart application and this communication was not received by any individual designated in 37 C.F.R. § 1.56(c) more than thirty days prior to the filing of this information disclosure statement.

■ 2. Filing under 37 C.F.R. § 1.97(b). This Information Disclosure Statement is being filed within three months of the date of filing of a national application other than a continued prosecution application (CPA), OR within three months of the date of entry of the national stage as set forth in 37 C.F.R. § 1.491 in an international application, OR before the mailing date of a first Office Action on the merits OR before the mailing of a first Office Action after the filing of a request for continued examination under 37 C.F.R. § 1.114. No statement or fee is required.

☐ 3. Filing under 37 C.F.R. § 1.97(c). This Information Disclosure Statement is being filed more than three months after the U.S. filing date AND after the mailing date of the first Office Action on the merits, but before the mailing date of a Final Rejection, or Notice of Allowance, or an action that otherwise closes prosecution in the application.

☐ a. Statement under 37 C.F.R. § 1.97(e)(1). I hereby state that each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement. 37 C.F.R. § 1.97(e)(1).

□ b. Statement under 37 C.F.R. § 1.97(e)(2). I hereby state that no item of information in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application and, to my knowledge after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Information Disclosure Statement. 37 C.F.R. § 1.97(e)(2).

□ c. Attached is our PTO-2038 Credit Card Payment Form in payment of the fee under 37 C.F.R. § 1.17(p).

□ 4. Filing under 37 C.F.R. § 1.97(d) This Information Disclosure Statement is being filed more than three months after the U.S. filing date and after the mailing date of a Final Rejection or Notice of Allowance, but before payment of the Issue Fee. Enclosed find our Check No. _____ in the amount of $ _____ in payment of the fee under 37 C.F.R. § 1.17(p); in addition:

□ a. Statement under 37 C.F.R. § 1.97(e)(1). I hereby state that each item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement. 37 C.F.R. § 1.97(e)(1).

□ b. Statement under 37 C.F.R. § 1.97(e)(2). I hereby state that no item of information in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application and, to my knowledge after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Information Disclosure Statement. 37 C.F.R. § 1.97(e)(2).

□ 5. The document(s) was/were cited in a search report by a foreign patent office in a counterpart foreign application. Submission of an English language version of the search report that indicates the degree of relevance found by the

foreign office is provided in satisfaction of the requirement for a concise explanation of relevance. 1138 OG 37, 38.

☐ 6. A concise explanation of the relevance of the non-English language document(s) appears below:

☐ 7. Copies of the documents were cited by or submitted to the Office in an IDS that complies with 37 C.F.R. § 1.98(a)-(c) in Application No. _____, filed _____, which is relied upon for an earlier filing date under 35 U.S.C. § 120. Thus, copies of these documents are not attached. 37 C.F.R. § 1.98(d).

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Virgil L. Beaston
Attorney for Applicants
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Date: 5/2/03

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•Practice Limited to Federal Agencies

May 2, 2003

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Art Unit 1631

Re: U.S. Non-Provisional Utility Patent
Appl. No. 10/058,216; Filed: January 29, 2002
For: **Method, System, and Computer Program Product for Analyzing Combinatorial Libraries**
Inventors: Agrafiotis *et al.*
Our Ref: 1503.1230001

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Third Supplemental Information Disclosure Statement;

2. Form PTO-1449 listing and accompanied by 195 documents; and

3. One return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Virgil L. Beaston
Attorney for Applicants
Registration No. 47,415

Enclosures

VLB/sjc
::ODMA\MHODMA\SKGF_DC1;130138;1

FORM PTO-1449 THIRD SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 1503.1230001	APPLICATION NO. 10/058,216
	APPLICANTS Agrafiotis et al.	
	FILING DATE January 29, 2002	GROUP 1631

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA1						
	AB1						
	AC1						
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	AI1						

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AJ1	EP 0 355 266 B1	02/1990	EPO	B01J	19/00	Yes No
	AK1	EP 0 355 628 B1	02/1990	EPO	G21F	9/00	Yes No
	AL1	EP 0 770 876 A1	05/1997	EPO	G01N	33/68	Yes No
	AM1	EP 0 818 744 A2	01/1998	EPO	G06F	17/50	Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	1	Borg, Ingwer and Groenen, Patrick, *Modern Multidimensional Scaling Theory and Applications*, Springer Series in Statistics, 1997, entire book submitted.
	AO	1	Agrafiotis, D.K. *et al.*, "Advances in diversity profiling and combinatorial series design," *Molecular Diversity*, Kluwer Academic Publishers, Vol. 4, 1999, pp. 1-22.
	AP	1	Agrafiotis, D.K. and Lobanov, V.S., "An Efficient Implementation of Distance-Based Diveristy Measures Based on *k-d* Trees," *Journal of Chemical Information and Computer Science*, American Chemical Society, Vol. 39, No. 1, January/February 1999, pp. 51-58.
	AQ	1	Agrafiotis, D.K. and Lobanov, V.S., "Bridging The Gap Between Diversity And QSAR," *Abstracts of Papers Part 1: 215th ACS National Meeting*, American Chemical Society, March 29-April 2, 1998, p. 181-COMP.
	AR	1	Agrafiotis, D.K. and Jaeger, E.P., "Directed Diversity®: An Operating System For Combinatorial Chemistry," *Abstracts of Papers Part 1: 211th ACS National Meeting*, American Chemical Society, March 24-28, 1996, p. 46-COMP.

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

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U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA2						
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AJ2	WO 91/19735	12/1991	PCT	C07K	7/02	Yes No
	AK2	WO 92/00091	01/1992	PCT	A61K	37/02	Yes No
	AL2	WO 93/20242	10/1993	PCT	C12Q	1/70	Yes No
	AM2	WO 94/28504	12/1994	PCT	G06F	15/60	Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	2	Agrafiotis, D.K., "Diversity of Chemical Libraries," *Encyclopedia of Computational Chemistry*, John Wiley & Sons Ltd, Vol. 1:A-D, 1998, pp. 742-761.
	AO	2	Agrafiotis, D.K., "On the Use of Information Theory for Assessing Molecular Diversity," *Journal of Chemical Information and Computer Science*, American Chemical Society, Vol. 37, No. 3, May/June 1997, pp. 576-580.
	AP	2	Agrafiotis, D.K. *et al.*, "Parallel QSAR," *Abstracts of Papers Part 1: 217th ACS National Meeting*, March 21-25, 1999, p. 50-COMP.
	AQ	2	Agrafiotis, D.K. *et al.*, "PRODEN: A New Program for Calculating Integrated Projected Populations," *Journal of Computational Chemistry*, John Wiley & Sons, Inc., Vol. 11, No. 9, October 1990, pp. 1101-1110.
	AR	2	Agrafiotis, D.K. and Jaeger, E.P., "Stochastic Algorithms for Exploring Molecular Diversity," *Abstracts of Papers Part 1: 213th ACS National Meeting*, American Chemical Society, April 13-17, 1997, p. 16-CINF.

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA3						
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AJ3	WO 95/01606	01/1995	PCT	G06F	15/42	Yes No
	AK3	WO 97/09342	03/1997	PCT	C07H	21/02	Yes No
	AL3	WO 97/20952	06/1997	PCT	C12Q	1/68	Yes No
	AM3	WO 97/27559	07/1997	PCT	G06F	19/00	Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	3	Agrafiotis, D., "Theoretical Aspects of the Complex: Arts and New Technologies," *Applications and Impacts Information Processing '94*, North-Holland, Vol. II, 1994, pp. 714-719.
	AO	3	Biswas, G. *et al.*, "Evaluation of Projection Algorithms," *IEEE Transactions On Pattern Analysis And Machine Intelligence*, IEEE Computer Society, Vol. PAMI-3, No. 6, November 1981, pp. 701-708.
	AP	3	Bonchev, D. and Trinajstić, N., "Information theory, distance matrix, and molecular branching," *The Journal of Chemical Physics*, American Institute of Physics, Vol. 67, No. 10, November 15, 1977, pp. 4517, 4520-4533.
	AQ	3	Chang, C.L. and Lee, R.C.T., "A Heuristic Relaxation Method for Nonlinear Mapping in Cluster Analysis," *IEEE Transactions on Systems, Man, and Cybernetics*, IEEE Systems, Man, and Cybernetics Society, Vol. SMC-3, March 1973, pp. 197-200.
	AR	3	Cramer, R.D. *et al.*, "Virtual Compound Libraries: A New Approach to Decision Making in Molecular Discovery Research," *J. Chem. Inf. Comput. Sci.*, American Chemical Society, Vol. 38, No. 6, November/December 1998, pp. 1010-1023.

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U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA4						
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AJ4	WO 98/20437	05/1998	PCT	G06F	17/50	Yes No
	AK4	WO 98/20459	05/1998	PCT	G06T	11/20	Yes No
	AL4						Yes No
	AM4						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	4	DeMers, D. and Cottrell, G., "Non-Linear Dimensionality Reduction," *Advances in Neural Information Processing Systems*, Vol. 5, 1993, pp. 580-587.
	AO	4	Frey, P.W. and Slate, D.J., "Letter Recognition Using Holland-Style Adaptive Classifiers," *Machine Learning*, Kluwer Academic Publishers, Vol. 6, 1991, pp. 161-182.
	AP	4	Friedman, J.H., "Exploratory Projection Pursuit," *Journal of the American Statistical Association*, American Statistical Association, Vol. 82, No. 397, March 1987, pp. 249-266.
	AQ	4	Friedman, J.H. and Tukey, J.W., "A Projection Pursuit Algorithm for Exploratory Data Analysis," *IEEE Transactions on Computers*, IEEE Computer Society, Vol. C-23, No. 9, September 1974, pp. 881-889.
	AR	4	Garrido, L. *et al.*, "Use of Multilayer Feedforward Neural Nets As A Display Method for Multidimensional Distributions," *International Journal of Neural Systems*, World Scientific Publishing Co. Pte. Ltd., Vol. 6, No. 3, September 1995, pp. 273-282.

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	APPLICANTS Agrafiotis *et al.*	
	FILING DATE January 29, 2002	GROUP 1631

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA5						
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AJ5						Yes No
	AK5						Yes No
	AL5						Yes No
	AM5						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	5	Ghose, A.K. *et al.*, "Prediction of Hydrophobic (Lipophilic) Properties of Small Organic Molecules Using Fragmental Methods: An Analysis of ALOGP and CLOGP Methods," *Journal of Physical Chemistry*, American Chemical Society, Vol. 102, No. 21, May 21, 1998, pp. 3762-3772.
	AO	5	Hall, L.H. and Kier, L.B., "The Molecular Connectivity Chi Indexes and Kappa Shape Indexes in Structure-Property Modeling," *Reviews in Computational Chemistry: Advances*, VCH Publishers, Inc., 1991, pp. 367-422.
	AP	5	Hecht-Nielsen, R., "Replicator Neural Networks for Universal Optimal Source Coding," *Science*, American Association for the Advancement of Science, Vol. 269, September 29, 1995, pp. 1860-1863.
	AQ	5	Hotelling, H., "Analysis of a Complex of Statistical Variables into Principal Components," *The Journal of Educational Psychology*, Warwick and York, Inc., Vol. XXIV, No. 6, September 1933, pp. 417-441.
	AR	5	Hotelling, H., "Analysis of a Complex of Statistical Variables into Principal Components," *The Journal of Educational Psychology*, Warwick and York, Inc., Vol. XXIV, No. 7, October 1933, pp. 498-520.

EXAMINER	DATE CONSIDERED

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA6						
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AJ6						No
	AK6						Yes No
	AL6						Yes No
	AM6						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	6	Lee, R.C.T. *et al.*, "A Triangulation Method for the Sequential Mapping of Points from *N*-Space to Two-Space," *IEEE Transactions on Computers*, The Institute of Electrical and Electronics Engineers, March 1977, pp. 288-292.
	AO	6	Lipinski, C.A. *et al.*, "Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings," *Advanced Drug Delivery Reviews*, Elsevier Science B.V., Vol. 23, 1997, pp. 3-25.
	AP	6	Lobanov, V.S. and Agrafiotis, D.K., "Intelligent Database Mining Techniques," *Abstracts of Papers Part 1: 215th ACS National Meeting*, March 29-April 2, 1998, p. 19-COMP.
	AQ	6	Lobanov, V.S. *et al.*, "Rational Selections from Virtual Libraries," *Abstracts of Papers Part 1: 217th ACS National Meeting*, March 21-25, 1999, p. 181-COMP.
	AR	6	Mao, J. and Jain, A.K., "Artificial Neural Networks for Feature Extraction and Multivariate Data Projection," *IEEE transactions on Neural Networks*, IEEE Neural Networks, Vol. 6, No. 2, March 1995, pp. 296-317.

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U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA7						
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AJ7						Yes No
	AK7						No
	AL7						Yes No
	AM7						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	7	Oja, E., "Principal Components, Minor Components, and Linear Neural Networks," *Neural Networks*, Pergamon Press Ltd., Vol. 5, 1992, pp. 927-935.
	AO	7	Patterson, D.E. *et al.*, "Neighborhood Behavior: A Useful Concept for Validation of 'Molecular Diversity' Descriptors," *Journal of Medicinal Chemistry*, American Chemical Society, Vol. 39, No. 16, 1996, pp. 3049-3059.
	AP	7	Pykett, C.E., "Improving the Efficiency of Sammon's Nonlinear Mapping by Using Clustering Archetypes," *Electronics Letters*, The Institution of Electrical Engineers, Vol. 14, No. 25, December 7, 1978, pp. 799-800.
	AQ	7	Rubner, J. and Tavan, P., "A Self-Organizing Network for Principal-Component Analysis," *Europhysics Letters*, European Physical Society, Vol. 10, No. 7, December 1, 1989, pp. 693-698.
	AR	7	Sadowski, J. *et al.*, "Assessing Similarity and Diversity of Combinatorial Libraries by Spatial Autocorrelation Functions and Neural Networks," *Angewandte Chemie*, VCH, Vol. 34, No. 23/24, January 5, 1996, pp. 2674-2677.

EXAMINER	DATE CONSIDERED

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FORM PTO-1449

THIRD SUPPLEMENTAL
INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.	APPLICATION NO.
1503.1230001	10/058,216
APPLICANTS: Agrafiotis *et al.*	
FILING DATE: January 29, 2002	GROUP: 1631

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA8						
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AJ8						No
	AK8						No
	AL8						No
	AM8						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	8	Thompson, L.A. and Ellman, J.A., "Synthesis and Applications of Small Molecule Libraries," *Chemical Reviews*, American Chemical Society, Vol. 96, No. 1, January/February 1996, pp. 555-585, 588-600.
	AO	8	Barnard, John M. and Downs, Geoff M., "Computer representation and manipulation of combinatorial libraries," *Perspectives in Drug Discovery and Design*, Kluwer Academic Publishers, 1997, pp. 13-30.
	AP	8	Brint, Andrew T. and Willett, Peter, "Upperbound procedures for the identification of similar three-dimensional chemical structures," *Journal of Computer-Aided Molecular Design*, ESCOM Science Publishers B.V., Vol. 2, No. 4, January 1989, pp. 311-320.
	AQ	8	Brown, Robert D. and Martin, Yvonne C., "Designing Combinatorial Library Mixtures Using a Genetic Algorithm," *Journal of Medicinal Chemistry*, American Chemical Society, Vol. 40, No. 15, 1997, pp. 2304-2313.
	AR	8	Kim, J. *et al.*, "Multiple Neural Networks using the Reduced Input Dimension," *Proceedings of the International Conference on Acoustics, Speech, and Signal Processing*, IEEE, Vol. 2, April 19-22, 1994, pages II-601 to II-604.

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FORM PTO-1449 THIRD SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 1503.1230001	APPLICATION NO. 10/058,216
	APPLICANTS Agrafiotis *et al.*	
	FILING DATE January 29, 2002	GROUP 1631

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA9						
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AJ9						Yes No
	AK9						Yes No
	AL9						Yes No
	AM9						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	9	Gillet, Valerie J. *et al.*, "Selecting Combinatorial Libraries to Optimize Diversity and Physical Properties," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, Vol. 39, No. 1, 1999, pp. 169-177.
	AO	9	Kearsley, Simon K. *et al.*, "Chemical Similarity Using Physiochemical Property Descriptors," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, Vol. 36, No. 1, 1996, pp. 118-127.
	AP	9	Leland, Burton A. *et al.*, "Managing the Combinatorial Explosion," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, Vol. 37, No. 1, 1997, pp. 62-70.
	AQ	9	Lewis, Richard A. *et al.*, "Similarity Measures for Rational Set Selection and Analysis of Combinatorial Libraries: The Diverse Property-Derived (DPD) Approach," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, Vol. 37, No. 3, 1997, pp. 599-614.
	AR	9	Martin, Eric J. and Critchlow, Roger E., "Beyond Mere Diversity: Tailoring Combinatorial Libraries for Drug Discovery," *Journal of Combinatorial Chemistry*, American Chemical Society, Vol. 1, No. 1, 1999, pp. 32-45.

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	AJ10						Yes No
	AK10						Yes No
	AL10						Yes No
	AM10						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	10	Sheridan, Robert P. *et al.*, "Chemical Similarity Using Geometric Atom Pair Descriptors," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, Vol. 36, No. 1, 1996, pp. 128-136.
	AO	10	Willett, Peter *et al.*, "Chemical Similarity Searching," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, Vol. 38, No. 6, 1998, pp. 983-996.
	AP	10	Agrafiotis, Dimitris K. and Lobanov, Victor S., "Ultrafast Algorithm for Designing Focused Combinational Arrays," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, 2000, Vol. 40, No. 4, pp. 1030-1038.
	AQ	10	Ajay *et al.*, "Can We Learn To Distinguish between 'Drug-Like' and 'Nondrug-like' Molecules?" *J. Med. Chem.*, 1998, American Chemical Society, Vol. 41, No. 18, pp. 3314-3324.
	AR	10	English-language Abstract of European Patent No. 0 355 628, printed from Dialog File No. 351(February, 1990 - Date of publication of application), 2 pages.

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	AJ11						Yes No
	AK11						Yes No
	AL11						Yes No
	AM11						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	11	Brown, Robert D. and Martin, Yvonne C., "The Information Content of 2D and 3D Structural Descriptors Relevant to Ligand-Receptor Binding," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, 1997, Vol. 37, No. 1, pp. 1-9.
	AO	11	Brown, Robert D. and Martin, Yvonne C., "Use of Structure-Activity Data To Compare Structure-Based Clustering Methods and Descriptors for Use in Compound Selection," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, 1996, Vol. 36, No. 3, pp. 572-584.
	AP	11	Cummins, David J. *et al.*, "Molecular Diversity in Chemical Databases: Comparison of Medicinal Chemistry Knowledge Bases and Databases of Commercially Available Compounds," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, 1996, Vol. 36, No. 4, pp. 750-763.
	AQ	11	Domine, D. *et al.*, "Non-Linear Mapping for Structure-Activity and Structure-Property Modelling," *Journal of Chemometrics*, John Wiley & Sons, Ltd., Vol. 7, No. 4, July-August 1993, pp. 227-242.
	AR	11	Havel, T., "A New Method for Building Protein Conformations from Sequence Alignments with Homologues of Known Structure," *Journal of Molecular Biology*, Academic Press Limited, Vol 217, No. 1, January 5, 1991, pages 1-7.

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	AJ12						
	AK12						
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	12	Downs, Geoff M. and Barnard, John M., "Techniques for Generating Descriptive Fingerprints in Combinatorial Libraries," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, 1997, Vol. 37, No. 1, pp. 59-61.
	AO	12	Gillet, Valerie J., "Background Theory of Molecular Diversity," *Molecular Diversity in Drug Design*, Kluwer Academic Publishers, 1999, pp. 43-65.
	AP	12	Good, Andrew C. and Lewis, Richard A., "New Methodology for Profiling Combinatorial Libraries and Screening Sets: Cleaning Up the Design Process with HARPick," *Journal of Medicinal Chemistry*, American Chemical Society, 1997, Vol. 40, No. 24, pp. 3926-3936.
	AQ	12	Pal, N.R. and Eluri, V.K., "Two Efficient Connectionist Schemes for Structure Preserving Dimensionality Reduction," *IEEE Transactions on Neural Networks*, IEEE, Vol 9, No. 6, November 1998, pp. 1142-1154.
	AR	12	Jamois, Eric A. *et al.*, "Evaluation of Reagent-Based and Product-Based Strategies in the Design of Combinatorial Library Subsets," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, 2000, Vol. 40, No.1, pp. 63-70.

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1503.1230001	10/058,216
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	AA13						
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	13	Kim, H. *et al.*, "Self-Organized Distributed Networks for Learning Highly Nonlinear Mapping," *Intelligent Engineering Systems Through Artificial Neural Networks*, American Society of Mechanical Engineers, Vol. 4, November 13-16, 1994, pp. 109-114.
	AO	13	Leach, Andrew R. *et al.*, "Implementation of a System for Reagent Selection and Library Enumeration, Profiling, and Design," *Jounal of Chemical Information and Computer Sciences*, American Chemical Society, 1999, Vol. 39, No. 6, pp. 1161-1172.
	AP	13	Lobanov, Victor S. and Agrafiotis, Dimitris K., "Stochastic Similarity Selections from Large Combinatorial Libraries," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, March/April 2000, Vol. 40, No. 2, pp. 460-470.
	AQ	13	Matter, Hans and Pötter, Thorsten, "Comparing 3D Pharmacophore Triplets and 2D Fingerprints for Selecting Diverse Compound Subsets," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, 1999, Vol. 39, No. 6, pp. 1211-1225.
	AR	13	Matter, Hans, "Selecting Optimally Diverse Compounds from Structure Databases: A Validation Study of Two-Dimensional and Three-Dimensional Molecular Descriptors," *Journal of Medicinal Chemistry*, American Chemical Society, 1997, Vol. 40, No. 8, pp. 1219-1229.

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	AA14						
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	AJ14						No
	AK14						No
	AL14						No
	AM14						No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	14	Sadowski, Jens and Kubinyi, Hugo, "A Scoring Scheme for Discriminating between Drugs and Nondrugs," *Journal of Medicinal Chemistry*, American Chemical Society, 1998, Vol. 41, No. 18, pp. 3325-3329.
	AO	14	Schnur, Dora, "Design and Diversity Analysis of Large Combinatorial Libraries Using Cell-Based Methods," *Journal of Chemical Information and Computer Science*, American Chemical Society, 1999, Vol. 39, No. 1, pp. 36-45.
	AP	14	Schuffenhauer, Ansgar *et al.*, "Similarity Searching in Files of Three-Dimensional Chemical Structures: Analysis of the BIOSTER Database Using Two-Dimensional Fingerprints and Molecular Field Descriptors," *Journal of Chemical Information and Computer Science*, American Chemical Society, 2000, Vol. 40, No. 2, pp. 295-307.
	AQ	14	Turner, David B. *et al.*, "Rapid Quantification of Molecular Diversity for Selective Database Acquisition," *Journal of Chemical Information and Computer Science*, American Chemical Society, 1997, Vol. 37, No. 1, pp. 18-22.
	AR	14	Wang, Jing and Ramnarayan, Kal, "Toward Designing Drug-Like Libraries: A Novel Computational Approach for Prediction of Drug Feasibility of Compounds," *Journal of Combinatorial Chemistry*, American Chemical Society, November/December 1999, Vol. 1, No. 6, pp. 524-533.

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	AJ15						No
	AK15						No
	AL15						No
	AM15						No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	15	Gasteiger, J. *et al*, "Assessment of the Diversity of Combinatorial Libraries by an Encoding of Molecular Surface Properties," *Abstracts of Papers Part 1: 211th ACS National Meeting*, March 24-28, 1996, p. 70-CINF.
	AO	15	Hassan, Moises *et al.*, "Optimization and visualization of molecular diversity of combinatorial libraries," *Molecular Diversity*, ESCOM Science Publishers B.V., 1996, Vol. 2, pp. 64-74.
	AP	15	Bellman, R.E., *Adaptive Control Processes: A Guided Tour*, Princeton Univ. Press, Princeton, NJ (1961), entire book submitted.
	AQ	15	Bezdek, J.C., *Pattern Recognition with Fuzzy Objective Function Algorithms*, Plenum Press, New York, NY (1981), entire book submitted.
	AR	15	Johnson, M.A., and Maggiora, G.M., *Concepts and Applications of Molecular Similarity*, John Wiley and Sons, New York, NY (1990), entire book submitted.

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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AJ16						No
	AK16						No
	AL16						No
	AM16						No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	16	Kohonen, T., *Self-Organizing Maps*, Springer-Verlag, Heidelberg, Germany (1995), entire book submitted.
	AO	16	Oja, E., *Subspace Methods of Pattern Recognition*, Research Studies Press Ltd., Letchworth, England (1983), entire book submitted.
	AP	16	Agrafiotis, D.K., "A New Method For Analyzing Protein Sequence Relationships Based On Sammon Maps," *Protein Science*, Cambridge University Press, Vol. 6, No. 2, February 1997, pp. 287-293.
	AQ	16	Spellmeyer, D. *et al.*, "Conformational analysis using distance geometry methods," *Journal of Molecular Graphics & Modelling*, Elsevier Science, Inc., Vol. 15, No. 1, February 1997, pages 18-36.
	AR	16	Amzel, L.M., "Structure-based drug design," *Current Opinion in Biotechnology*, Vol. 9, No. 4, August 1998, pp. 366-369.

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	AJ17						No
	AK17						No
	AL17						No
	AM17						No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	17	Blaney, J.M. and Martin, E.J., "Computational approaches for combinatorial library design and molecular diversity analysis," *Current Opinion in Chemical Biology*, Current Biology Ltd., Vol. 1, No. 1, June 1997, pp. 54-59.
	AO	17	Saunders, M. , "Stochastic Exploration of Molecular Mechanics Energy Surfaces. Hunting for the Global Minimum," *Journal of the American Chemical Society*, American Chemical Society, Vol. 109, 10, May 13, 1987, pages 3150-3152.
	AP	17	Caflisch, A. and Karplus, M., "Computational combinatorial chemistry for de novo ligand design: Review and assessment," *Perspectives in Drug Discovery and Design*, ESCOM Science Publishers B.V., Vol. 3, 1995, pp. 51-84.
	AQ	17	Porto, V. *et al.*, "Alternative Neural Network Training Methods," *IEEE Expert*, IEEE, Vol. 10, No. 4, pages 16-22.
	AR	17	Eichler, U. *et al.*, "Addressing the problem of molecular diversity," *Drugs of the Future*, Prous Science, Vol. 24, No. 2, 1999, pp. 177-190.

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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AJ18						Yes No
	AK18						Yes No
	AL18						Yes No
	AM18						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	18	Felder, E.R. and Poppinger, D., "Combinatorial Compound Libraries for Enhanced Drug Discovery Approaches," *Advances in Drug Research*, Academic Press, Vol. 30, 1997, pp. 112-199.
	AO	18	Geysen, H.M. and Mason, T.J., "Screening Chemically Synthesized Peptide Libraries for Biologically-Relevant Molecules," *Bioorganic & Medicinal Chemistry Letters*, Pergamon Press Ltd., Vol. 3, No. 3, 1993, pp. 397-404.
	AP	18	Gobbi, A. *et al.*, "New Leads By Selective Screening of Compounds From Large Databases," *Abstracts of Papers Part 1: 213th ACS National Meeting*, American Chemical Society, April 13-17, 1997, p. 67-CINF.
	AQ	18	Houghten, R.A. *et al.*, "The Use of Synthetic Peptide Combinatorial Libraries for the Identification of Bioactive Peptides," *Peptide Research*, Vol. 5, No. 6, 1992, pp. 351-358.
	AR	18	Klopman, G., "Artificial Intelligence Approach to Structure-Activity Studies. Computer Automated Structure Evaluation of Biological Activity of Organic Molecules," *Journal of the American Chemical Society*, American Chemical Society, Vol. 106, No. 24, 1984, pp. 7315-7321.

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	AJ19						Yes No
	AK19						Yes No
	AL19						Yes No
	AM19						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	19	Lajiness, M.S. *et al.*, "Implementing Drug Screening Programs Using Molecular Similarity Methods," *QSAR: Quantitative Structure-Activity Relationships in Drug Design*, Alan R. Liss, Inc., 1989, pp. 173-176.
	AO	19	Loew, G.H. *et al.*, "Strategies for Indirect Computer-Aided Drug Design," *Pharmaceutical Research*, Plenum Publishing Corporation, Vol. 10, No. 4, 1993, pp. 475-486.
	AP	19	Lynch, M.F. *et al.*, "Generic Structure Storage and Retrieval," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, Vol. 25, No. 3, August 1985, pp. 264-270.
	AQ	19	Myers, P.L. *et al.*, "Rapid, Reliable Drug Discovery," *Today's Chemist At Work*, American Chemical Society, Vol. 6, No. 7, July/August 1997, pp. 46-48, 51 & 53.
	AR	19	Pabo, C.O. and Suchanek, E.G., "Computer-Aided Model-Building Strategies for Protein Design," *Biochemistry*, American Chemical Society, Vol. 25, No. 20, 1986, pp. 5987-5991.

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	AJ20						Yes No
	AK20						Yes No
	AL20						Yes No
	AM20						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	20	Saudek, V. *et al.*, "Solution Conformation of Endothelin-1 by H NMR, CD, and Molecular Modeling," *International Journal of Peptide Protein Research*, Munksgaard International Publishers Ltd., Vol. 37, No. 3, 1991, pp. 174-179.
	AO	20	Singh, J. *et al.*, "Application of Genetic Algorithms to Combinatorial Synthesis: A Computational Approach to Lead Identification and Lead Optimization," *J. Am. Chem. Soc.*, American Chemical Society, Vol. 118, No. 7, February 7, 1996, pp. 1669-1676.
	AP	20	Van Drie, J.H. and Lajiness, M.S., "Approaches to virtual library design," *Drug Discovery today*, Elsevier Science Ltd., Vol. 3, No. 6, June 1998, pp. 274-283.
	AQ	20	Walters, W.P. *et al.*, "Virtual screening - an overview," *Drug Discovery today*, Elsevier Science Ltd., Vol. 3, No. 4, April 1998, pp. 160-178.
	AR	20	Weber, L., "Evolutionary combinatorial chemistry: application of genetic algorithms," *Drug Discovery today*, Elsevier Science Ltd., Vol. 3, No. 8, August 1998, pp. 379-385.

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	AJ21						Yes No
	AK21						Yes No
	AL21						Yes No
	AM21						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	21	Weber, L. *et al.*, "Optimization of the Biological Activity of Combinatorial Compound Libraries by a Genetic Algorithm," *Angewandte Chemie International Edition in English*, VCH, Vol. 34, No. 20, November 3, 1995, pp. 2280-2282.
	AO	21	Graybill, T.L. *et al.*, "Enhancing the Drug Discovery Process by Integration of High-Throughput Chemistry and Structure-Based Drug Design," Molecular Diversity and Combinatorial Chemistry: Libraries and Drug Discovery, American Chemical Society, 1996, pp. 16-27.
	AP	21	Saund, E., "Dimensionality-Reduction Using Connectionist Networks," *IEEE Transactions on Pattern Analysis and Machine Intelligence*, IEEE, Vol. 11, No. 3, March 1989, pp. 304-314.
	AQ	21	"3DP gains drug research patent", *Chemistry in Britain*, The Royal Society of Chemistry, Vol. 32, No. 1, January 1996, p. 22.
	AR	21	"Accelerate the Discovery Cycle with Chem-X!", Source and date of publication unclear, 2 pages.

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FORM PTO-1449 THIRD SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 1503.1230001	APPLICATION NO. 10/058,216
	APPLICANTS Agrafiotis *et al.*	
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U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AJ22						Yes No
	AK22						Yes No
	AL22						Yes No
	AM22						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	22	Agrafiotis, D. K., "Stochastic Algorithms for Maximizing Molecular Diversity", *Journal of Chemical Information and Computer Sciences,* American Chemical Society, Vol. 37, No. 5, 1997, pp. 841-851.
	AO	22	Alsberg, B.K. *et al.*, "Classification of pyrolysis mass spectra by fuzzy multivariate rule induction-comparison with regression, *K*-nearest neighbour, neural and decision-tree methods", *Analytica Chimica Acta*, Elsevier Science B.V., Vol. 348, No. 1-3, August 20, 1997, pp. 389-407.
	AP	22	Andrea, T.A. and Kalayeh, H., "Applications of Neural Networks in Quantitative Structure-Activity Relationships of Dihydrofolate Reductase Inhibitors", *Journal of Medicinal Chemistry*, American Chemical Society, Vol. 34, No. 9, 1991, pp. 2824-2836.
	AQ	22	Aoyama, T. *et al.*, "Neural Networks Applied to Quantitative Structure-Activity Relationship Analysis", *Journal of Medicinal Chemistry*, American Chemical Society, Vol. 33, No. 9, 1990, pp. 2583-2590.
	AR	22	Aoyama, T. and Ichikawa, H., "Obtaining the Correlation Indices between Drug Activity and Structural Parameters Using a Neural Network", *Chemical & Pharmaceutical Bulletin*, Pharmaceutical Society of Japan, Vol. 39, No. 2, February 1991, pp. 372-378.

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	AJ23						Yes No
	AK23						Yes No
	AL23						Yes No
	AM23						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	23	Mumenthaler, Ch. And Braun, W., "Automated Assignment of Simulated and Experimental NOESY Spectra of Proteins by Feedback Filtering and Self-correcting Distance Geometry," *Journal of Molecular Biology,* Academic Press Limited, Vol. 254, No. 3, December 1, 1995, pages 465-480.
	AO	23	Baum, R.M., "Combinatorial Approaches Provide Fresh Leads for Medicinal Chemistry", *Chemical & Engineering News*, American Chemical Society, February 7, 1994, pp. 20-26.
	AP	23	Bentley, J. L., "Multidimensional Binary Search Trees Used for Associative Searching", *Communications of the ACM*, Association for Computing Machinery, Inc., Vol. 18, No. 9, September 1975, pp. 509-517.
	AQ	23	Bottou, L. and Vapnik, V. "Local Learning Algorithms", *Neural Computation*, Massachusetts Institute of Technology, Vol. 4, No. 6, November 1992, pp. 888-900.
	AR	23	Boulu, L.G. and Crippen, G.M., "Voronoi Binding Site Models: Calculation of Binding Modes and Influence of Drug Binding Data Accuracy", *Journal of Computational Chemistry*, John Wiley & Sons, Inc., Vol. 10, No. 5, July/August 1989, pp. 673-682.

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	AJ24						Yes No
	AK24						Yes No
	AL24						Yes No
	AM24						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	24	Boulu, L.G. *et al.*, "Voronoi Binding Site Model of a Polycyclic Aromatic Hydrocarbon Binding Protein", *Journal of Medicinal Chemistry*, American Chemical Society, Vol. 33, No. 2, 1990, pp. 771-775.
	AO	24	Cacoullos, T., "Estimation of a Multivariate Density", *Annals of The Institute of Statistical Mathematics*, The Institute of Statistical Mathematics, Vol. 18, No. 2, 1966, pp. 179-189.
	AP	24	Clark, R.D., "OptiSim: An Extended Dissimilarity Selection Method for Finding Diverse Representative Subsets", *Journal of Chemical Information and Computer Sciences*, American Chemical Society, Vol. 37, No. 6, 1997, pp. 1181-1188.
	AQ	24	Clark, D. E., and Westhead, D.R., "Evolutionary algorithms in computer-aided molecular design", *Journal of Computer-Aided Molecular Design*, ESCOM Science Publishers B.V., Vol. 10, No. 4, August 1996, pp. 337-358.
	AR	24	Cramer, III, R. D. *et al.*, "Comparative Molecular Field Analysis (CoMFA). 1. Effect of Shape on Binding of Steroids to Carrier Proteins", *Journal of The American Chemical Society*, American Chemical Society, Vol. 110, No. 18, August 31, 1988, pp. 5959-5967.

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	AJ25						Yes No
	AK25						Yes No
	AL25						Yes No
	AM25						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	25	Cramer, III, R. D. *et al.*, "Substructural Analysis. A Novel Approach to the Problem of Drug Design", *Journal of Medicinal Chemistry*, Vol. 17, No. 5, May 1974, pp. 533-535.
	AO	25	Crippen, G. M., "Voronoi Binding Site Models", *Journal of Computational Chemistry*, John Wiley & Sons, Inc., Vol. 8, No. 7, October/November 1987, pp. 943-955.
	AP	25	Friedman, J. H. *et al.*, "An Algorithm for Finding Best Matches in Logarithmic Expected Time", *ACM Transactions on Mathematical Software*, Association for Computing Machinery, Vol. 3, No. 3, September 1977, pp. 209-226.
	AQ	25	Friedman, J.H., "Fitting Functions To Noisy Data In High Dimensions", Department of Statistics- Stanford University Technical Report No. 101, (August, 1988), pages 1-36.
	AR	25	Gallop, M. A. *et al.*, "Applications of Combinatorial Technologies to Drug Discovery. 1. Background and Peptide Combinatorial Libraries", *Journal of Medicinal Chemistry*, American Chemical Society, Vol. 37, No. 9, April 29, 1994, pp. 1233-1251.

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	AA26						
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	AJ26						Yes No
	AK26						Yes No
	AL26						Yes No
	AM26						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	26	Ghose, A. K. and Crippen, G.M., "Use of Physicochemical Parameters in Distance Geometry and Related Three-Dimensional Quantitative Structure-Activity Relationships: A Demonstration Using *Escherichia coli* Dihydrofolate Reductase Inhibitors", *Journal of Medicinal Chemistry*, American Chemical Society, Vol. 28, No. 3, 1985, pp. 333-346.
	AO	26	Good, A. C. *et al.*, "Structure-Activity Relationships from Molecular Similarity Matrices", *Journal of Medicinal Chemistry*, American Chemical Society, Vol. 36, No. 4, February 19, 1993, pp. 433-438.
	AP	26	Gordon, E. M. *et al.*, "Applications of Combinatorial Technologies to Drug Discovery. 2. Combinatorial Organic Synthesis, Library Screening Strategies, and Future Directions", *Journal of Medicinal Chemistry*, American Chemical Society, Vol. 37, No. 10, May 13, 1994, pp. 1385-1401.
	AQ	26	Hartigan, J. A., "Representation of Similarity Matrices By Trees", *Journal of the American Statistical Association*, Vol. 62, No. 320, December, 1967, pp. 1140-1158.
	AR	26	Hopfinger, A. J., "A QSAR Investigation of Dihydrofolate Reductase Inhibition by Baker Triazines Based upon Molecular Shape Analysis", *Journal of the American Chemical Society*, American Chemical Society, Vol. 102, No. 24, November 19, 1980, pp. 7196-7206.

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	AJ27						Yes No
	AK27						Yes No
	AL27						Yes No
	AM27						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	27	Jackson, R. C., "Update on computer-aided drug design", *Current Opinion in BIOTECHNOLOGY*, Current Biology Ltd., Vol. 6, No. 6, December 1995, pp. 646-651.
	AO	27	Kim, K. H., "Comparative molecular field analysis (CoMFA)", *Molecular Similarity in Drug Design*, ed. P. M. Dean, Blackie Academic & Professional, 1995, Ch. 12, pp. 291-331.
	AP	27	Kohonen, T., "Self-Organized Formation of Topologically Correct Feature Maps", *Biological Cybernetics*, Springer-Verlag, Vol. 43, No. 1, 1982, pp. 59-69.
	AQ	27	Koile, K. and Shapiro, R., "Building A Collaborative Drug Design System", *Proceedings of the 25h Hawaii International Conference on System Sciences*, IEEE, 1992, pp. 706-716.
	AR	27	Kowalski, B. R. and Bender, C. F., "Pattern Recognition. II. Linear and Nonlinear Methods for Displaying Chemical Data", *Journal of the American Chemical Society*, American Chemical Society, Vol. 95, No. 3, February 7, 1973, pp. 686-693.

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	AJ28						Yes No
	AK28						Yes No
	AL28						Yes No
	AM28						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	28	Kruskal, J. B., "Nonmetric Multidimensional Scaling: A Numerical Method", *Psychometrika*, Vol. 29, No. 2, June, 1964, pp. 115-129.
	AO	28	Lengauer, T. and Rarey, M., "Computational methods for biomolecular docking", *Current Opinion in Structural Biology*, Current Biology Ltd, Vol. 6, No. 3, June, 1996, pp. 402-406.
	AP	28	Luke, B. T., "Evolutionary Programming Applied to the Development of Quantitative Structure-Activity Relationships and Quantitative Structure-Property Relationships", *Journal of Chemical Information and Computer Sciences*, American Chemical Society, Vol. 34, No. 6, November/December 1994, pp. 1279-1287.
	AQ	28	Martin, E. J. *et al.*, "Does Combinatorial Chemistry Obviate Computer-Aided Drug Design?", *Reviews in Computational Chemistry*, VCH Publishers, Inc., Vol. 10, 1997, pp. 75-99.
	AR	28	Martin, E. J. *et al.*, "Measuring Diversity: Experimental Design of Combinatorial Libraries for Drug Discovery", *Journal of Medicinal Chemistry*, American Chemical Society, Vol. 38, No. 9, April 28, 1995, pp. 1431-1436.

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	AJ29						Yes No
	AK29						Yes No
	AL29						Yes No
	AM29						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	29	McMartin, C. and Bohacek, R.S., "QXP: Powerful, rapid computer algorithms for structure-based drug design", *Journal of Computer-Aided Molecular Design*, Kluwer Academic Publishers, Vol. 11, No. 4, July 1997, pp. 333-344.
	AO	29	Mezey, P. G. and Walker, P.D., "Fuzzy molecular fragments in drug research", *Drug Discovery today,* Vol. 2, No. 4, April 1997, pp. 132-137.
	AP	29	Müller, K., "On the paradigm shift from rational to random design", *Journal of Molecular Structure (Theochem)*, Elsevier Science B.V., Vol. 398-399, Special Issue, 1997, pp. 467-471.
	AQ	29	Havel, T. and Wüthrich, K., "An Evaluation of the Combined Use of Nuclear Magnetic Resonance and Distance Geometry for the Determination of Protein Conformations in Solution," *Journal of Molecular Biology*, Academic Press Inc., Vol. 182, No. 2, March 20, 1985, pages 281-294.
	AR	29	Meng, E. *et al.*, "Orientational Sampling and Rigid-Body Minimization in Molecular Docking," *PROTEINS: Structure, Function and Genetics*, Wiley-Liss, Inc., Vol. 17, No. 3, 1993, pages 266-278.

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	AJ30						Yes No
	AK30						Yes No
	AL30						Yes No
	AM30						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	30	Omohundro, S. M., "Bumptrees for Efficient Function, Constraint, and Classification Learning", *Advances in Neural Information Processing Systems 3*, Morgan Kaufmann, 1991, 7 pages, unknown.
	AO	30	Parrill, A. L., "Evolutionary and genetic methods in drug design", *Drug Discovery today*, Elsevier Science Ltd., Vol. 1, No. 12, December 1996, pp. 514-521.
	AP	30	Polanski, J., "A neural network for the simulation of biological systems", *Journal of Molecular Structure (Theochem)*, Elsevier Science Ltd., Vol. 398-399, Special Issue, 1997, pp. 565-571.
	AQ	30	Ramos-Nino, M. E. *et al.*, "A comparison of quantitative structure-activity relationships for the effect of benzoic and cinnamic acids on *Listeria monocytogenes* using multiple linear regression, artificial neural network and fuzzy systems", *Journal of Applied Microbiology*, Society for Applied Bacteriology, Vol. 82, No. 2, February 1997, pp. 168-176.
	AR	30	Rogers, D. and Hopfinger, A. J., "Application of Genetic Function Approximation to Quantitative Structure-Activity Relationships and Quantitative Structure-Property Relationships", *Journal of Chemical Information and Computer Sciences*, American Chemical Society, Vol. 34, No. 4, July/August 1994, pp. 854-866.

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	AJ31						Yes No
	AK31						Yes No
	AL31						Yes No
	AM31						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	31	Sammon, Jr., J. W., "A Nonlinear Mapping for Data Structure Analysis", *IEEE Transactions on Computers*, IEEE, Vol. C-18, No. 5, May 1969, pp. 401-409.
	AO	31	Simon, Z. *et al.*, "Mapping of Dihydrofolate-reductase Receptor Site by Correlation with Minimal Topological (Steric) Differences", *Journal of Theoretical Biology*, Academic Press, Inc., Vol. 66, No. 3, June 7, 1997, pp. 485-495.
	AP	31	Smellie, A. S. *et al.*, "Fast Drug-Receptor Mapping by Site-Directed Distances: A Novel Method of Predicting New Pharmacological Leads", *Journal of Chemical Information and Computer Sciences*, American Chemical Society, Vol. 31, No.3, August 1991, pp. 386-392.
	AQ	31	Specht, D. F., "A General Regression Neural Network", *IEEE Transactions on Neural Networks*, IEEE, Vol. 2, No. 6, November 1991, pp. 568-576.
	AR	31	Svozil, D. *et al.*, "Neural Network Prediction of the Solvatochromic Polarity/Polarizability Parameter π^{H}_{2}", *Journal of Chemical Information and Computer Sciences*, American Chemical Society, Vol. 37, No. 2, 1997, pp. 338-342.

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	AJ32						Yes No
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	AL32						Yes No
	AM32						Yes No

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	AN	32	Todorov, N. P. and Dean, P. M., "Evaluation of a method for controlling molecular scaffold diversity in de novo ligand design", *Journal of Computer-Aided Molecular Design*, ESCOM Science Publishers B.V., Vol. 11, 1997, pp. 175-192.
	AO	32	Torgerson, W. S., "Multidimensional Scaling: I. Theory and Method", *Psychometrika*, The Psychometric Society, Vol. 17, No. 4, December 1952, pp. 401-419.
	AP	32	Vapnik, V., "Principles of Risk Minimization for Learning Theory", *Advances in Neural Information Processing Systems 4*, Morgan Kaufmann Publishers, Inc., 1992, pp. 831-838.
	AQ	32	Vapnik, V. and Bottou, L., "Local Algorithms for Pattern Recognition and Dependencies Estimation", *Neural Computation*, Massachusetts Institute of Technology, Vol. 5, No. 6, November 1993, pp. 893-909.
	AR	32	Viswanadhan, V. N. *et al.*, "Mapping the binding site of the nucleoside transporter protein: a 3D-QSAR study", *Biochimica et Biophysica Acta*, Elsevier Science Publishers B.V., Vol. 1039, No. 3, 1990, pp. 356-366.

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	AK33						Yes No
	AL33						Yes No
	AM33						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	33	Kuszewski, J. *et al.*, "Sampling and efficiency of metric matrix, distance geometry: A novel partial metrization algorithm," *Journal of Biomolecular NMR*, Escom Science Publishers B.V., Vol. 2, No. 1, January 1992, pages 33-56.
	AO	33	Westhead, D. R. *et al.*, "A comparison of heuristic search algorithms for molecular docking", *Journal of Computer-Aided Molecular Design*, Kluwer Academic Publishers, Vol. 11, 1997, pp. 209-228.
	AP	33	Willett, P., "Genetic algorithms in molecular recognition and design", *Trends in Biotechnology*, Elsevier Science Publishers B.V., Vol, 13, No. 12, December 1995, pp. 516-521.
	AQ	33	Willett, P. and Winterman, V., "A Comparison of Some Measures for the Determination of Inter-Molecular Structural Similarity Measures of Inter-Molecular Structural Similarity", *Quantitative Structure-Activity Relationships*, VCH, Vol. 5, No. 1, March 1986, pp. 18-25.
	AR	33	Zadeh, L. A., "Communication Fuzzy Algorithms", *Information and Control*, Academic Press Inc., Vol. 12, No. 2, February 1968, pp. 94-102.

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FORM PTO-1449 THIRD SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 1503.1230001	APPLICATION NO. 10/058,216
	APPLICANTS Agrafiotis et al.	
	FILING DATE January 29, 2002	GROUP 1631

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA34						
	AB34						
	AC34						
	AD34						
	AE34						
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	AG34						
	AH34						
	AI34						

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AJ34						Yes No
	AK34						Yes No
	AL34						Yes No
	AM34						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	34	Zadeh, L. A., "Fuzzy Sets", *Information and Control*, Academic Press Inc., Vol. 8, No. 3, June 1965, pp. 338-353.
	AO	34	Jorgensen, W. and Tirado-Rives, J., "Monte Carlo vs. Molecular Dynamics for Conformational Sampling," *Journal of Physical Chemistry*, American Chemical Society, Vol. 100, No. 34, August 22, 1996, pages 14508-14513.
	AP	34	Jain, A. *et al.*, "Artificial Neural Networks: A Tutorial," IEEE, March 1996, pages 31-44.
	AQ	34	Aoyama, T. *et al.*, "Neural Networks Applied to Structure-Activity Relationships," *Journal of Medicinal Chemistry*, American Chemical Society, Vol. 33., No. 3, 1990, pp. 905-908.
	AR	34	Gasteiger, J. *et al.*, "Analysis of the Reactivity of Single Bonds in Aliphatic Molecules by Statistical and Pattern Recognition Methods," *Journal of Chemical Information and Computer Sciences*, American Chemical Society, Vol. 33, No. 3, 1993, pp. 385-394.

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

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	AA35						
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	AJ35						Yes No
	AK35						Yes No
	AL35						Yes No
	AM35						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	35	Guez, A. and Nevo, I., "Neural networks and fuzzy logic in clinical laboratory computing with application to integrated monitoring," *Clinica Chimica Acta*, Elsevier Science Publishers B.V., Vol. 248, 1996, pp. 73-90.
	AO	35	Rouvray, D.H., "Similarity in Chemistry: Past, Present and Future," *Topics in Chemistry*, Springer-Verlag, Vol. 173, 1995, pp. 1-30.
	AP	35	de Ridder, D. and Duin, R.P.W., "Sammon's mapping using neural networks: A comparison," *Pattern Recognition Letters*, Elsevier Science Publishers B.V., Vol. 18, No. 11-13, 1997, pp. 1307-1316.
	AQ	35	Havel, T. and Wüthrich, K., " A Distance Geometry Program for Determining the Structures of Small Proteins and other Macromolecules from Nuclear Magnetic Resonance Measurements of Intramolecular ^{1}H- ^{1}H Proximities in Solution," *Bulletin of Mathematical Biology*, Pergamon Press, Vol. 46, No. 4, 1984, pages 673-698.
	AR	35	Chang, G. et al., "An Internal Coordinate Monte Carlo Method for Searching Conformational Space, *Journal of the American Chemical Society*, American Chemical Society, Vol. III, June 1989, No. 12, pages 4379-4386.

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	AA36						
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	AJ36						Yes No
	AK36						Yes No
	AL36						Yes No
	AM36						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	36	Crippen, G.M. and Havel, T.F., *Distance Geometry and Molecular Conformation*, Research Studies Press Ltd., 1988, entire book submitted.
	AO	36	Feuston, B. *et al.*, "Comparison of Knowledge-Based and Distance Geometry Approaches for Generation of Molecular Conformations," *Journal of Information and Computer Sciences*, American Chemical Society, Vol. 41, No. 3, 2001, pages 754-763.
	AP	36	Ferguson, D. and Raber, D., "A New Approach to Probing Conformational Space with Molecular Mechanics: Random Incremental Pulse Search," *Journal of the American Chemical Society*, American Chemical Society, Vol. 111, No. 12, 1989, pages 4371-4378.
	AQ	36	Halgren, T. and Nachbar, R., "Merck Molecular Force Field. IV. Conformational Energies and Geometries for MMFF94*," *Journal of Computational Chemistry*, John Wiley & Sons, Inc., Vol. 17, Nos. 5 & 6, 1996, pages 587-915.
	AR	36	Halgren, T., "Merck Molecular Force Field. V. Extension of MMFF94 Using Experimental Data, Additional Computational Data, and Empirical Rules*," *Journal of Computational Chemistry*, John Wiley & Sons, Inc., Vol. 17, Nos. 5 & 6, April 1996, pages 616-641.

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	AJ37						Yes No
	AK37						Yes No
	AL37						Yes No
	AM37						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AN	37	Huang, E. et al., "Distance geometry generates native-like folds for small helical proteins using the consensus distances of predicted protein structures," *Protein Science*, The Protein Society, Vol. 7, No. 9, September 1998, pages 1998-2003.
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	AR	37	

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